

TOBACCO SMOKING AND CANCER OF THE LUNG

*Statement by the Medical Research Council**

The Increase in Lung Cancer

In their Annual Report for 1948-50 the Council drew attention to the very great increase that had taken place in the death rate from lung cancer over the previous twenty-five years. Since that time, the death rate has continued to rise, and in 1955 it reached a level more than double that recorded only ten years earlier (388 deaths per million of the population in 1955 compared with 188 in 1945). Among males the disease is now responsible for approximately 1 in 18 of all deaths. Although the death rate for females is still comparatively low, it also has shown a considerable increase in recent years and the disease is now responsible for 1 in 103 of all female deaths.

Three comments may be made on these figures. In the first place, the trend over the last few years indicates that the incidence has not yet reached its peak. Secondly, the figures are not to be explained as a mere reflection of the introduction and increasing use of improved methods of diagnosis but must be accepted as representing, in the main, a real rise in the incidence of the disease, to an extent which has occurred with no other form of cancer. Thirdly, only a small part of the rise can be attributed to the larger numbers of older persons now living in the population; in the last ten years the lung cancer death rates among both men and women have risen at all ages from early middle-life onwards.

Possible Causes of the Increase

The extent and rapidity of the increase in lung cancer point clearly to some potent environmental influence which has become prevalent in the past half-century and to which different countries, and presumably also men as compared with women, have been unequally exposed. The pattern of incidence of the disease rules out any possibility that the increase can be due, in a substantial degree, to special conditions, such as occupational hazards, affecting only limited groups. It is necessary to seek some factor or factors distributed generally throughout the population, and in considering the possibilities it must be borne in mind that a very long period, 20 years or more, may elapse between exposure to a carcinogenic agent and the production of a tumour. From the nature of the disease attention has focussed on two main environmental factors: (1) the smoking of tobacco, and (2) atmospheric pollution—whether from homes, factories, or the internal combustion engine.

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Smoking as a Cause of Lung Cancer

(a) Epidemiological Surveys

The evidence that heavy and prolonged smoking of tobacco, particularly in the form of cigarettes, is associated with an increased risk of lung cancer is not based on the observation that the substantial increase in the national mortality followed an increase in the national consumption of cigarettes. It is derived from two types of special inquiry. In the first, patients with lung cancer have been interviewed and their *previous* histories in relation to smoking and other factors that might be relevant have been compared with those similarly obtained from patients without lung cancer. The results of nineteen such inquiries (in this country, the U.S.A., Finland, Germany, Holland, Norway and Switzerland) have been published. They agree in showing more smokers and fewer non-smokers among the patients with lung cancer, and a steadily rising mortality as the amount of smoking increases. In the second type of inquiry, information has been obtained about the smoking habits of each member of a defined group in the population and the causes of the deaths occurring *subsequently* in the group have been ascertained. There have been two such investigations, one in the U.S.A. covering 190,000 men aged 50-69, and the other in this country covering over 40,000 men and women whose names appeared on the Medical Register of 1951. In both, the results have been essentially the same. The investigation in this country, which has now been in progress for more than five years, has shown with regard to lung cancer in men :—

- (1) a higher mortality in smokers than in non-smokers ;
- (2) a higher mortality in heavy smokers than in light smokers ;
- (3) a higher mortality in cigarette smokers than in pipe smokers ;
- (4) a higher mortality in those who continued to smoke than in those who gave it up.

It follows that the highest mortalities were found among men who were continuing to smoke cigarettes, heavy smokers in this group having a death rate nearly 40 times the rate among non-smokers. Although no precise calculation can be made of the proportion of life-long heavy cigarette smokers who will die of lung cancer, the evidence suggests that, at current death rates, it is likely to be of the order of 1 in 8, whereas the corresponding figure for non-smokers would be of the order of 1 in 300. The observation on the effect of giving up smoking is particularly important, since it indicates that men who cease to smoke, even in their early forties, may reduce their likelihood of developing the disease by at least one half.

It should be noted that the excess of deaths from lung cancer among smokers was not compensated for by any corresponding reduction in the number of deaths from cancer of other sites in the body ; in other words, there was a total incidence of cancer in the smoking groups in excess of the incidence that would have prevailed in the absence of smoking.

It will be apparent from what has been said that the evidence from the many inquiries in the last eight years, both in this country and abroad, has been uniformly in one direction and is now very considerable. It has been further strengthened recently by the observation from several sources that the extent of the relationship with smoking differs for different types of lung tumour which can be distinguished only by microscopic examination.

(b) Laboratory Evidence

From the physical and chemical point of view there is nothing inherently improbable in a connection between smoking and lung cancer. Tobacco smoke consists largely of microscopic oily droplets held in suspension in air, and these droplets are of a suitable size to be taken into the lungs and retained there. Over a hundred constituents have so far been identified and, among these, five substances have already been found which are known to be capable, in certain circumstances, of causing cancer in animals. Some workers have succeeded in producing tumours in animals by painting concentrated extracts of tobacco tar on the skin. Known carcinogens are present in tobacco smoke in very small amounts however, and there is no certainty that such low concentrations could be harmful to human beings. Nevertheless, the finding of carcinogenic agents in tobacco smoke is an important step forward, in that it provides a rational basis for the hypothesis of causation.

Atmospheric Pollution as a Cause of Lung Cancer

It has been known for some years that mortality from lung cancer is greater in urban areas than in the countryside. This fact, together with the identification of carcinogenic substances in coal smoke and in motor vehicle exhausts, has led to the supposition that exposure to atmospheric pollution may be concerned with the increase in lung cancer. The role of atmospheric pollution is particularly difficult to investigate however, and the evidence is neither so consistent nor so extensive as that relating to tobacco smoking. On the one hand, no excess mortality from lung cancer has been observed in persons who would be especially exposed by the nature of their work to atmospheric pollution, for example transport workers, garage hands and policemen. On the other hand, the results of a number of investigations have suggested that a relationship does exist between atmospheric pollution and lung cancer. Perhaps the best evidence for this relationship comes from studies of the small number of deaths from the disease among *non-smokers* in different types of residential district; in these studies higher death rates have been observed among non-smokers in large towns than among those in rural areas. On balance it seems likely that atmospheric pollution plays some part in causing the disease, but a relatively minor one in comparison with cigarette smoking.

Assessment of the Evidence Relating to Smoking and Lung Cancer

Knowledge of the causation of lung cancer is still incomplete. Many factors other than tobacco smoking are undoubtedly capable of producing the disease; for example, at least five industrial causes have been recognised. Nevertheless, the evidence for an association between lung cancer and tobacco smoking has been steadily mounting throughout the past 8 years and it is significant that, during the whole of this period, the most critical examination has failed to invalidate the main conclusions drawn from it. It has indeed been suggested that the fundamental cause may be some common factor underlying both the tendency to tobacco smoking and to the development of lung cancer some 25 to 50 years later, but no evidence has been produced in support of this hypothesis.

In scientific work, as in the practical affairs of everyday life, conclusions have often to be founded on the most reasonable and probable explanation of the observed facts and, so far, no adequate explanation for the large increase in the incidence of lung cancer has been advanced save that cigarette smoking is indeed the principal factor in the causation of the disease. The epidemiological evidence is now extensive and very detailed, and it follows a classical pattern upon which many advances in preventive medicine have been made in the past. It is clearly impossible to add to the evidence by means of an experiment in man. The Council are, however, supporting a substantial amount of laboratory research which may throw more light on the mechanism by which tobacco smoke and other suspected causative factors exert their effect, and which may thus eventually add to the degree of proof already attained as a result of studies of human populations. It must be emphasised, however, that negative results from work with animals cannot invalidate conclusions drawn from observations on man.

Conclusions

1. A very great increase has occurred during the past 25 years in the death rate from lung cancer in Great Britain and other countries.
2. A relatively small number of the total cases can be attributed to specific industrial hazards.
3. A proportion of cases, the exact extent of which cannot yet be defined, may be due to atmospheric pollution.
4. Evidence from many investigations in different countries indicates that a major part of the increase is associated with tobacco smoking, particularly in the form of cigarettes. In the opinion of the Council, the most reasonable interpretation of this evidence is that the relationship is one of direct cause and effect.
5. The identification of several carcinogenic substances in tobacco smoke provides a rational basis for such a causal relationship.

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